DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

December 10, 1997

Our Reference No.: 97-0736

Ms. Loni da Silva
Hoffmann-La Roche Inc.
340 Kingsland Street
Building 1, 2nd floor
Nutley, NJ 07110-1199

Dear Ms. da Silva:

Your biologics license application for Daclizumab is approved effective this date. Hoffmann-La Roche Inc., Nutley, New Jersey is hereby authorized to manufacture and ship for sale, barter, or exchange in interstate and foreign commerce Daclizumab under Department of Health and Human Services Biologics License No. 0136.

Daclizumab is indicated for the prophylaxis of acute organ rejection in patients receiving renal transplants, to be used as a part of an immunosuppressive regimen that includes cyclosporine and corticosteroids.

In accordance with approved labeling, your product will bear the tradename Zenapax, and will be marketed in 5 ml single-use vials containing 25 mg of Daclizumab.

You are not currently required to submit samples of future lots of Daclizumab to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2. FDA will continue to monitor compliance with 21 CFR 610.1 requiring assay and release of only those lots that meet release specifications.

The dating period for this product shall be 12 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated product. The purified, unformulated bulk Daclizumab may be stored up to 9 months from the date of manufacture when stored at either 2-8°C or -80°C. Results of ongoing stability studies should be submitted throughout the dating period as they become available including the results of stability studies from the first three production lots.

We acknowledge your written commitments of December 10, 1997, regarding the following product and clinical issues:

1. To revise, within three months, the drug substance release method [~~~~~~~~~~] to improve the description of the pass/fail criteria.

(b)(4)

2. To submit, by June 1999, the results of a three-year follow-up analysis of the Phase 3 studies including the incidence of acute and chronic rejection and patient and graft survival rates.

3. To submit, upon completion, the results of ongoing studies of Daclizumab use in pediatric patients.

4. To submit, within 60 days, a draft protocol for a study to evaluate the incidence and duration of impairment, if any, of the immune response to new and recall foreign antigen(s) in patients receiving Daclizumab.

5. To submit supplements to modify the package insert to reflect these additional data as they become available.

Any changes in the manufacture, packaging or labeling of the product or in the manufacturing facilities will require the submission of information to your biologics license application for our review and written approval consistent with 21 CFR 601.12.

It is requested that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit three copies of all final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567. All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Sincerely yours,

Jay P. Siegel, M.D., FACP
Director
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research